

The Development of the MeDALL Core Questionnaires for a Harmonized Follow-Up Assessment of Eleven European Birth Cohorts on Asthma and Allergies

Cynthia Hohmann^a Mariona Pinart^{b–d, h} Christina Tischer^e Ulrike Gehring¹ Joachim Heinrich^e
Inger Kull^{g, w, x} Eric Melén^{g, x} Henriette A. Smit^y Maties Torrent^{d, z} Alet H. Wijga^f Magnus Wickman^{g, x}
Claus Bachertⁱ Karin C. Lødrup Carlsen^j Kai-Håkon Carlsen^j Carsten Bindslev-Jensen^k Esben Eller^k
Ana Esplugues^{d, l, m} Maria Pia Fantiniⁿ Isabella Annesi-Maesano^o Isabelle Momas^{p, q} Daniela Porta^r
Maria Vassilaki^s Dagmar Waiblinger^t Jordi Sunyer^{b–d, h} Josep M. Antó^{b–d, h} Jean Bousquet^{u, v}
Thomas Keil^{a, 2} The MeDALL Study Group

^aInstitute of Social Medicine, Epidemiology and Health Economics, Charité – Universitätsmedizin Berlin, Germany; ^bCentre for Research in Environmental Epidemiology (CREAL), ^cIMIM (Hospital del Mar Medical Research Institute), and ^dCIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain; ^eInstitute of Epidemiology, German Research Centre for Environmental Health, Helmholtz Zentrum München, Neuherberg, Germany; ^fCentre for Prevention and Health Services Research, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands; ^gInstitute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; ^hUniversitat Pompeu Fabra (UPF), Departament de Ciències Experimentals i de la Salut, Barcelona, Spain; ⁱUpper Airway Research Laboratory, University of Ghent, Ghent, Belgium; ^jDepartment of Paediatrics, Oslo University Hospital and University of Oslo, Oslo, Norway; ^kDepartment of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark; ^lDivision of Environment and Health, Centre for Public Health Research – CSISP, and ^mFaculty of Nursing, University of Valencia, Valencia, Spain; ⁿDepartment of Medicine and Public Health, Alma Mater Studiorum, University of Bologna, Bologna, Italy; ^oEPAR U707 INSERM, and EPAR UMR-S UPMC, Paris VI, ^pDepartment of Public Health and Biostatistics, Paris Descartes University, EA 4064, and ^qParis Municipal Department of Social Action, Childhood and Health, Paris, France; ^rDepartment of Epidemiology, Regional Health Service Lazio Region, Rome, Italy; ^sDepartment of Social Medicine, Faculty of Medicine, University of Crete, Heraklion, Greece; ^tBradford Institute for Health Research, Bradford Teaching Hospitals Foundation Trust, and Bradford Neonatology, Bradford Royal Infirmary, Bradford, UK; ^uUniversity Hospital, Department of Respiratory Diseases, Hôpital Arnaud de Villeneuve, Montpellier, and ^vInserm, CESP Centre for Research in Epidemiology and Population Health, U1018, Respiratory and Environmental Epidemiology team, Villejuif, France; ^wDepartment of Clinical Science and Education, Karolinska Institutet, and ^xSachs' Children's Hospital, Stockholm, Sweden; ^yJulius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands; ^zMenorca Health Area, Ib-Salut, Mahon, Spain; ¹Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands; ²Institute of Clinical Epidemiology and Biometry, University of Würzburg, Würzburg, Germany

Key Words

European birth cohorts · Asthma · Allergy · Questionnaire assessment · Harmonization · MeDALL

Abstract

Background: Numerous birth cohorts have been initiated in the world over the past 30 years using heterogeneous methods to assess the incidence, course and risk factors of

asthma and allergies. The aim of the present work is to provide the stepwise proceedings of the development and current version of the harmonized MeDALL-Core Questionnaire (MeDALL-CQ) used prospectively in 11 European birth cohorts. **Methods:** The harmonization of questions was accomplished in 4 steps: (i) collection of variables from 14 birth cohorts, (ii) consensus on questionnaire items, (iii) translation and back-translation of the harmonized English MeDALL-CQ into 8 other languages and (iv) implementa-

tion of the harmonized follow-up. **Results:** Three harmonized MeDALL-CQs (2 for parents of children aged 4–9 and 14–18, 1 for adolescents aged 14–18) were developed and used for a harmonized follow-up assessment of 11 European birth cohorts on asthma and allergies with over 13,000 children. **Conclusions:** The harmonized MeDALL follow-up produced more comparable data across different cohorts and countries in Europe and will offer the possibility to verify results of former cohort analyses. Thus, MeDALL can become the starting point to stringently plan, conduct and support future common asthma and allergy research initiatives in Europe.

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Introduction

Numerous cohorts focusing on asthma and allergy have been initiated in the world over the past 30 years, most of them focusing on the evaluation of incidence, course and risk factors of asthma and allergies [1, 2]. In Europe, the costs of persistent asthma were estimated at EUR 19.3 billion and most costs were due to young patients aged 15–30 years [3]. The questionnaires used by many cohorts to assess symptoms of asthma and rhinitis included several questions based on those developed and validated in the worldwide International Study of Asthma and Allergies in Childhood (ISAAC) [4]. Although the order and/or wording of the ISAAC questions were usually slightly modified, questions on asthma and allergic rhinitis were homogeneously assessed across European birth cohorts. On the other hand, the assessment of other allergic phenotypes (e.g. eczema, sensitization to aero- and food allergens), pulmonary development and possible determinants of allergic diseases, including dietary habits and environmental exposures, were rather heterogeneous [1, 2]. MeDALL attempts to increase the amount of harmonized questions beyond those included in the ISAAC questionnaire or those which might have been included in the ISAAC questionnaire but were not frequently used by the cohorts in the last years.

Since 2004, several research initiatives funded under the EU Framework Program for Research and Technological Development FP6-FP7 have attempted to identify, compare and evaluate pooled data from existing European birth cohorts [5]: GA²LEN (Global Allergy and European Network, FP6) [6], ENRIECO (Environmental Health Risks in European Birth Cohorts, FP7) [7], CHICOS (Developing a Child Cohort Research

Strategy for Europe, FP7) and MeDALL (Mechanisms of the Development of Allergy, FP7) [8–10]. Combined analyses across birth cohorts result in larger sample sizes and increased statistical power, and broaden the diversity of environmental exposure assessments and facilitate research on underlying mechanisms explaining heterogeneous results among the cohorts [11].

Combining birth cohort data can be done retrospectively on historical data or prospectively by using the same core questionnaire and standard operating procedures for physical examinations. The collaborative MeDALL project aims to integrate epidemiological and clinical research and to identify inherited and environmental factors associated with the onset of allergy in children [8, 9]. Within this project, combined analyses of historical data from 14 European birth cohorts are underway. Moreover, MeDALL harmonizes a core assessment for follow-up of 11 birth cohorts in order to prospectively collect data on asthma and allergies. It is of importance that historical and prospective questions are interoperable to compare data.

Questionnaires for birth cohorts are collected according to the age at examination. In adolescents questionnaires are completed by the participants and their parents, whereas in school children (under 10 years) questionnaires are given to the parents only. In MeDALL, participants of 8 birth cohorts are older than 13 years (in the following referred to as the ‘older birth cohorts’) and participants of 6 others are younger than 10 years (in the following referred to as the ‘younger birth cohorts’) at the time of the harmonized follow-up.

The aim of the present work is to provide the stepwise proceedings of the development and current version of the MeDALL-Core Questionnaire (MeDALL-CQ) used prospectively in over 13,000 children. More specifically: (1) different working steps and the item selection process for the harmonized MeDALL-CQ are described and (2) the 3 English MeDALL-CQs, namely the parental (MeDALL-PQ, 14–18 years) and adolescent (MeDALL-AQ, 14–18 years) versions for the older birth cohorts and the parental questionnaire (MeDALL-PQ, 4–9 years) for the younger birth cohorts are presented in the online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000357732). (3) Translations in 8 languages and standard operating procedures for clinical examinations are available but not included in the present paper. They can be retrieved by contacting the corresponding author. The harmonized MeDALL follow-up is ongoing and resulting data will be presented in following publications.

Table 1. The eight birth cohorts (participant age 14–18 years) that took part in the development of a harmonized MeDALL-CQ

Birth cohort	Country/region	Year of recruitment	Size at recruitment, n	Age at MeDALL follow-up, years	Size at MeDALL follow-up (expected), n
BAMSE	Sweden/Stockholm	1994–1996	4,089	16–18	3,300
PIAMA-NHS	The Netherlands/North, West and Central	1996–1997	3,963	15–17	2,500
GINIplus	Germany/Munich, Wesel	1996–1998	5,991	14–17	2,050
LISApplus	Germany/Munich, Wesel, Leipzig, Bad Honnef	1997–1998	3,097	15–17	1,050
AMICS-Menorca	Spain/Menorca	1997–1998	485	14–15	380
DARC	Denmark/Odense	1998–1999	562	14–15	450
ECA	Norway/Oslo	1992–1993	3,754	16–17	550
MAS	Germany/Berlin, Düsseldorf, Mainz, Freiburg, Munich	1990	1,314	20	790

Six of the cohorts took part in the common MeDALL follow-up assessment and two birth cohorts (ECA, MAS) had a follow-up based on own funding.

Table 2. The six birth cohorts (participant age 4–9 years) that took part in the development of a harmonized MeDALL-CQ and the common MeDALL follow-up assessment

Birth cohort	Country/region	Year of recruitment	Size at recruitment, n	Age at MeDALL follow-up, years	Size at MeDALL follow-up (expected), n
BiB	UK/Bradford	2007–2010	13,776	4	1,500
INMA	Spain/Valencia, Sabadell, Guipuzkoa	2004–2008	3,768	4–7	1,100
PARIS	France/Paris	2003–2006	4,115	8	900
RHEA	Greece/Heraklion, Crete	2007–2008	1,497	4	900
ROBBIC	Italy/Rome,	2003	709	8–9	700
	Italy/Bologna	2003	654		
EDEN	France/Nancy, Poitiers	2003–2006	1,896	5	900

Five of the cohorts took part in the common MeDALL follow-up assessment and one birth cohort (EDEN) had a follow-up based on own funding, which did not use the MeDALL-CQ.

Materials and Methods

Members of MeDALL-CQ

Members of 8 older European MeDALL birth cohorts (AMICS-Menorca, BAMSE, DARC, ECA, GINIplus, LISApplus, MAS and PIAMA-NHS) developed and approved a common harmonized MeDALL-CQ for adolescent participants (MeDALL-AQ, 14–18 years) and their parents (MeDALL-PQ, 14–18 years; table 1).

Members of 6 younger European MeDALL birth cohorts (BiB, EDEN, INMA, PARIS, ROBBIC and RHEA) developed and approved a common harmonized MeDALL-PQ, for children aged 4–9 years (table 2).

Development of MeDALL-CQ

The harmonization of questions was conducted for 8 major sections (table 3) in 4 steps: (i) collection of variables from 14 birth cohorts, (ii) consensus on questionnaire items, (iii) translation and

back-translation of the harmonized English MeDALL-CQ in 8 other languages and (iv) implementation of the harmonized follow-up (fig. 1).

During the process, it was important to reach a consensus on the inclusion of the questionnaire items by achieving a maximal harmonization between the cohorts and, at the same time, not to endanger longitudinal comparisons within each cohort. The MeDALL-CQ included core questions but also shared additional questions and gave the cohorts the opportunity to include a number of their own individual questions. This questionnaire, available in 9 different languages, was used prospectively by 11 MeDALL birth cohorts.

Sections and Item Selection for the MeDALL-CQ

Health Outcomes

The definitions for asthma, rhinitis and eczema were based on a MeDALL consensus meeting held in Barcelona, June 2011 [12].

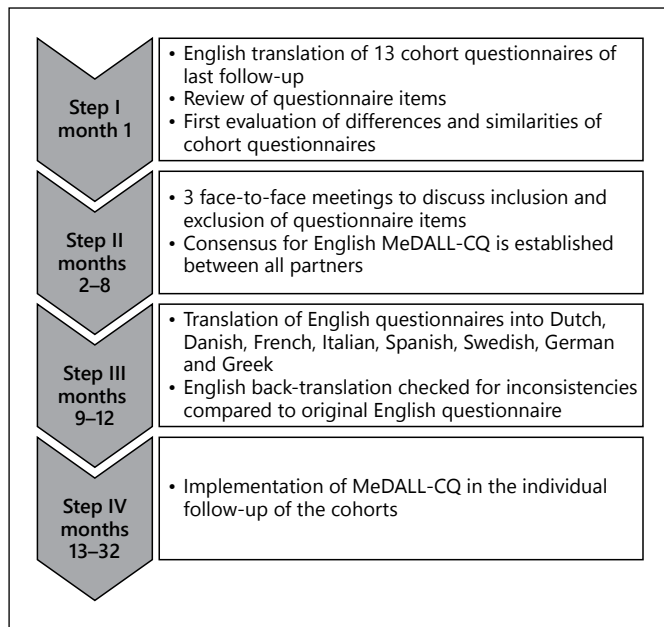


Fig. 1. Overview of the different working steps of the development of the harmonized MeDALL-Core Questionnaires (CQ) currently used by 11 European birth cohorts.

Table 3. Major sections of the common MeDALL questionnaire

1. Asthma
2. Allergic rhinitis
3. Eczema
4. Socio-demographic questions
5. Nutrition
6. Indoor environment (dampness/mold, tobacco smoke exposure, air pollution)
7. Lifestyle factors (physical activity, smoking, alcohol and drugs)
8. Puberty development

Asthma. ISAAC questions on wheezing symptoms [4], questions on doctor's diagnosis, hospital visits and medication intake were chosen to assess the prevalence and severity of asthma. Based on the decisions of the working group the adolescent core questionnaire, AQ, contained additional questions on tightness of chest and shortness of breath since these symptoms are also considered as 'key indicators for considering a diagnosis of asthma' [13]. The triad of respiratory symptoms (wheezing and/or tightness of chest and/or shortness of breath), doctor's diagnosis and medication intake was used for a questionnaire-based definition of asthma in children and adolescents [8, 14, 15]. In the MeDALL-AQ, a visual analog scale was used to estimate asthma and its impact on daily life, as these scales are more sensitive to small outcome differences than, for example, ordinal scales are [16], and may be relevant to assess the control of asthma [8]. Depending on country-specific

differences, the wording of the question regarding an asthma diagnosis by a doctor might be adapted (e.g. additional questions for doctor's diagnosis of obstructive, asthmatic or spastic bronchitis for German-speaking countries). Questions for which it was unclear whether the judgment about the illness was based on a doctor's diagnosis or on self-diagnosis were not incorporated. Moreover, the MeDALL-CQs gave the cohorts the opportunity to include a number of cohort-specific questions to allow for consistency with earlier follow-ups. For the asthma section, this comprises questions on seasonal variations of symptoms, chronic obstructive lung disease and further details of medication intake. These questions were included in the section for optional use.

Rhinitis. The presence of rhinitis can be assessed by questionnaire assessment, while allergic rhinitis can be assessed by a questionnaire on nasal symptoms and the demonstration of an IgE-mediated sensitization to specific allergens (using skin-prick testing and/or specific serum IgE assays) only. Seasonal and perennial rhinitis were distinguished by the inclusion of ISAAC questions on current (last 12 months) and seasonal rhinitis symptoms [4]. In addition, questions about medication use and prior allergen-specific immunotherapy were included. If only current symptoms are assessed, children with medication intake might wrongly be categorized as healthy because the extent of their currently experienced symptoms might be profoundly reduced by the treatment received. Questions based on ARIA were used to assess the duration and severity of allergic rhinitis [17]. In the MeDALL-AQ, 14–18 years, questions on rhinosinusitis were included based on suggestions in the European Position Paper on Rhinosinusitis and Nasal Polyps (EP³OS) emphasizing the importance of the current lack of knowledge about the incidence and prevalence of rhinosinusitis in European countries, and the need for 'large-scale epidemiologic research' [18, 19].

Eczema. The diagnosis of eczema by a doctor and the prevalence, severity and seasonal variations of eczema symptoms were assessed by means of items from the ISAAC questionnaire [4] and the Williams' and UK working criteria [20]. Moreover, questions on contact dermatitis were included. Concerning eczema severity, the POEM (Patient-Oriented Eczema Measure) [21] was part of the supplemental questionnaire which assesses self-reported recent eczema severity over the last 7 days. As for wheezing and rhinitis symptoms in epidemiological studies, the corresponding POEM-based eczema severity questions referred to the last 12 months. This method of assessing self-reported eczema severity will be validated by two of the birth cohorts during the course of MeDALL (BAMSE and DARC).

Possible Determinants of Allergic Diseases

Parental Allergies. Family history is a relevant risk factor of allergic diseases and regular assessments of parental allergies are necessary to record different patterns which might influence children's allergies [22]. Thus, the MeDALL-PQ contains questions on the diagnosis of asthma, rhinitis and eczema of both parents, also including age at onset of the disease and the differentiation between the doctor's diagnosis and self-diagnosis. Although information on parental allergies was already collected in former questionnaires (for most cohorts at birth) the differentiation between a self-diagnosis versus a doctor's diagnosis was lacking in most cohorts.

Nutrition. The birth cohorts participating in MeDALL are geographically spread across the European continent from Norway

and Sweden in the north to Spain and Greece in the south, covering various climatic and cultural regions with heterogeneous nutritional habits [23, 24]. Due to these considerable differences in diet among the MeDALL birth cohort study participants, and also reflected by the different instruments used in previous nutritional assessments in each of the cohorts, harmonized food questions could not be identified. However, all MeDALL cohorts assessed data on the food-item level by using cohort-specific food frequency questionnaires. Common questions for the MeDALL-CQs were agreed upon by the MeDALL partners to assess self- and parent-reported allergic reactions to food, including the age at first reaction, the type of allergic reaction and current allergic reactions to food items.

Indoor Environment. 'Cooking with gas' was included in the MeDALL-PQ and the inclusion of variables such as kitchen ventilation or the 'presence of other sources of combustion products' were not expected to explain additional variance when investigating respiratory health outcomes [25]. Three questions on 'dampness and/or mold within the home' were adapted from the LISA-plus and GINIplus cohorts aiming to follow-up a previous meta-analysis that suggested a possible link with wheezing and allergic rhinitis [15]. The parents were considered to be a more reliable source of information concerning the indoor environment at home than the adolescents. Active and passive tobacco smoke exposure, however, needed to be included in both the parental MeDALL-PQ as well as the adolescent MeDALL-AQ, since parents are not likely to know (exactly) their teenaged children's tobacco exposure outside the home.

Lifestyle Factors. In the MeDALL-AQ, 14–18 years, questions on physical activity, smoking, alcohol and drug consumption were included. For this purpose, the International Physical Activity Questionnaire (IPAQ) [26] was adapted to the needs of an epidemiological study. Instead of asking for physical activity during the last 7 days, which could be useful in cross-sectional or short-term intervention studies, the corresponding IPAQ-based MeDALL questions asked for physical activity during a typical week in the last 12 months in summer and, separately, in winter. It is planned to validate this assessment in the German LISA birth cohort by using accelerometers. Besides active smoking, questions on passive smoking at indoor locations were added to the MeDALL-PQ, distinguishing between second-hand smoke exposures 'at home' and 'not at home'. Alcohol and drug consumption were assessed each by two questions asking for the type of alcohol/drug and the amount of intake as glasses per week or times of intake in the last 12 months, adapted from the KiGGS survey [27]. The unit 'number of sips' used before by some of the cohorts was not considered as a valid proxy for current drinking behavior in adolescents. No consensus was reached about questions on binge drinking, but the following 2 questions were recommended for optional use: 'have you ever drunk that much alcohol that you have been dizzy or sick afterwards? If yes, how often in the last 12 months?' and 'have you ever drunk that much alcohol that you could not remember everything from the day before?', which have been used in former questionnaires by the cohorts GINIplus and LISApplus.

Puberty Development. In the MeDALL-ACQ, puberty development was assessed by the Pubertal Development Scale (PDS) [28]. The prospectively collected data since birth in the MeDALL cohorts provides the unique possibility to investigate determinants of the postulated sex-switch in the prevalence of asthma and allergic diseases during puberty [29].

Other Questions. The MeDALL-AQ contained questions on height, weight and school degree/level of schooling of the adolescent participants. Although allergies might play a minor role in adolescents' job choices [30], items inquiring whether the choice of schooling programs is affected by allergic diseases were included so that the prevalence of current allergic symptoms would not be underestimated due to the avoidance of known allergens. Furthermore, this question could give an idea of the severity of the allergic disease and its impact on the choices of the adolescent regarding everyday life. The items of this section were extracted from former cohort questionnaires and agreed on by all MeDALL birth cohorts.

Results

The three MeDALL-CQs consisted of 8 sections, of which each was divided into a core section and supplementary questions which remained optional for the cohorts. The complete MeDALL-CQs are presented in online supplementary figure 1–3. Please see online supplementary figure 4 for references of the single items of the MeDALL-CQs.

The MeDALL-AQ, 14–18 years, included 66 core-section items and 19 optional items for adolescents (online suppl. fig. 1). The parent-reported MeDALL-PQ, 14–18 years, included 50 core-section items and 5 optional items (online suppl. fig. 2). The parent-reported MeDALL-PQ, 4–9 years, included 56 core-section items and 37 optional items (online suppl. fig. 3).

Discussion

The MeDALL-CQ is, to our knowledge, the first attempt to develop a multilingual common core questionnaire for birth cohorts in allergy and asthma. It has been constructed using a rigorous stepwise process and it is now used in 11 birth cohorts in 9 European countries. It can be expanded to other countries in the world with relatively minor adaptation. This MeDALL-CQ is interoperable with historical data of the 14 MeDALL cohorts, making it possible to compare part of the data across several time points (table 4).

Limitations

In some sections of the questionnaire country-specific differences were so profound, for example in the section on nutrition, that it was decided that harmonization was impossible. Also, questions about educational status had to be adapted for each country. The other sections were judged to be suitable for the harmonization process and

Table 4. Interoperability table for relevant outcome and exposure variables for historical cohort data and harmonized data (MeDALL follow-up, last column) assessed from all cohorts at the MeDALL follow-up

Variables	Follow-up																
	<1 year	1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years	11 years	12 years	13 years	14 years	15 years	McDALL follow-up
<i>Asthma</i>																	
Wheeze	Amics-M, BAMSE, DARC, ECA, INMA-S, LISA, MAS, PARIS, PIAMA, RHEA, ROBBIC	Amics-M, BAMSE, DARC, ECA, EDEN, INMA-S, INMA-V, GINI, LISA, MAS, PIAMA, ROBBIC	Amics-M, BAMSE, DARC, EDEN, INMA-S, INMA-V, GINI, LISA, MAS, PIAMA, ROBBIC	Amics-M, BAMSE, DARC, EDEN, INMA-S, INMA-V, GINI, LISA, MAS, PIAMA, ROBBIC	Amics-M, BAMSE, EDEN, MAS, PARIS, PIAMA	EDEN, MAS, PARIS, PIAMA	Amics-M, DARC, GINI, LISA, MAS, PARIS, PIAMA	MAS, PIAMA	EDEN, PIAMA, MAS, BAMSE	Amics-M, MAS, BAMSE	LISA, MAS, ECA, BAMSE, GINI	PIAMA, BAMSE	BAMSE, MAS	MAS			✓
Chest tightness, shortness of breath	INMA-S, RHEA, ROBBIC	BIB, INMA-S, ROBBIC	INMA-S, ROBBIC	PARIS, PIAMA	INMA-S, PARIS, PIAMA	PARIS, PIAMA	PARIS, PIAMA	PIAMA	PIAMA			PIAMA					✓
Asthma medication	BAMSE, BIB, DARC, ECA, EDEN	Amics-M, BAMSE, BIB, DARC, ECA, EDEN, PIAMA	Amics-M, BAMSE, BIB, ECA, EDEN, PARIS, PIAMA	Amics-M, BAMSE, BIB, DARC, EDEN, GINI, PIAMA, ROBBIC	Amics-M, BAMSE, EDEN, INMA-V, PIAMA	EDEN, INMA-V, PIAMA	Amics-M, DARC, GINI, LISA, PIAMA	PIAMA	BAMSE, EDEN, MAS, PIAMA	Amics-M, MAS	ECA, GINI, MAS	BAMSE, MAS, PIAMA	BAMSE, MAS	MAS			✓
Doctor's diagnosis	BAMSE, BIB, DARC, ECA, EDEN, MAS, RHEA, ROBBIC	Amics-M, BAMSE, BIB, DARC, ECA, EDEN, GINI, LISA, MAS, PIAMA, ROBBIC	Amics-M, BAMSE, BIB, ECA, EDEN, GINI, LISA, MAS, PIAMA, ROBBIC	Amics-M, BAMSE, BIB, DARC, EDEN, MAS, PIAMA, ROBBIC	Amics-M, BAMSE, EDEN, INMA-V, GINI, LISA, MAS, PIAMA	BAMSE, EDEN, INMA-V, LISA, GINI, PARIS, PIAMA	Amics-M, BAMSE, DARC, GINI, LISA, MAS, PIAMA	BAMSE, GINI, LISA, MAS, PIAMA	BAMSE, EDEN, GINI, LISA, MAS, PIAMA	Amics-M, BAMSE, GINI, LISA, MAS	BAMSE, ECA, GINI, LISA, MAS	BAMSE, MAS, PIAMA	BAMSE, MAS	MAS			✓
<i>Eczema</i>																	
Dry skin	BAMSE, DARC, INMA-S	Amics-M, BAMSE, DARC, INMA-S	BAMSE, Amics-M, INMA-S, PARIS	Amics-M, DARC	Amics-M, INMA-V	Amics-M, DARC	Amics-M, DARC		BAMSE, Amics-M								✓
Itchy rash	Amics-M, BAMSE, EDEN, DARC, INMA-S, MAS, LISA, RHEA, ROBBIC	Amics-M, BAMSE, EDEN, DARC, GINI, INMA-S, MAS, LISA, MAS, PIAMA, ROBBIC	Amics-M, BAMSE, BIB, EDEN, GINI, INMA-S, MAS, LISA, MAS, PIAMA, ROBBIC	Amics-M, DARC, GINI, MAS, PIAMA, ROBBIC	Amics-M, BAMSE, EDEN, INMA-V, GINI, LISA, MAS, PIAMA	EDEN, MAS, PARIS, PIAMA	Amics-M, DARC, GINI, LISA, MAS, PIAMA	MAS, PIAMA	BAMSE, EDEN, MAS, PIAMA	Amics-M, MAS	GINI, LISA, MAS	MAS	BAMSE, MAS	MAS			✓

Table 4. (continued)

Variables	Follow-up															MedALL follow-up	
	<1 year	1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years	11 years	12 years	13 years	14 years		15 years
Itchy rash at flexural body parts	Amics-M, BAMSE, DARC, EDEN, INMA-S, LISA, PIAMA	Amics-M, BAMSE, DARC, EDEN, INMA-S, GINI, INMA-V, PARIS, PIAMA	Amics-M, BAMSE, GINI, INMA-S, INMA-V, PARIS, PIAMA	Amics-M, DARC, EDEN, GINI, INMA-V, PARIS, PIAMA	BAMSE, EDEN, GINI, INMA-V, LISA, MAS, PARIS, PIAMA	Amics-M, EDEN, MAS, PIAMA	Amics-M, DARC, GINI, LISA, MAS, PARIS, PIAMA	PIAMA	BAMSE, EDEN, PIAMA	Amics-M, GINI, LISA	GINI, LISA	PIAMA	BAMSE				✓
Rhinitis																	
	DARC, MAS, RHEA, ROBBIC	Amics-M, DARC, GINI, LISA, MAS, PARIS, ROBBIC	BIB, EDEN, GINI, LISA, MAS, PARIS	Amics-M, DARC, EDEN, GINI, MAS, PARIS, PIAMA, ROBBIC	Amics-M, BAMSE, EDEN, GINI, LISA, MAS, PARIS, PIAMA	MAS, PARIS, PIAMA	Amics-M, DARC, GINI, LISA, MAS, PARIS, PIAMA	MAS, PIAMA	BAMSE, EDEN, MAS, PIAMA	Amics-M, MAS	GINI, LISA, MAS	MAS, PIAMA	BAMSE, MAS				✓
Food allergy																	
	BAMSE, DARC, EDEN, INMA-S, LISA, MAS, PARIS, RHEA	BAMSE, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA	Amics-M, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA	Amics-M, DARC, EDEN, GINI, LISA, MAS, PARIS, PIAMA	BAMSE, EDEN, GINI, INMA-V, LISA, MAS, PARIS, PIAMA	BAMSE, EDEN, GINI, LISA, MAS, PARIS, PIAMA	BAMSE, DARC, GINI, LISA, MAS, PARIS, PIAMA	BAMSE, GINI, LISA, MAS, PIAMA	BAMSE, EDEN, GINI, LISA, MAS, PIAMA	GINI, LISA, MAS	GINI, LISA, MAS	MAS, PIAMA	MAS	BAMSE, MAS			✓
Smoking																	
	Amics-M, BAMSE, BIB, DARC, EDEN, GINI, LISA, MAS, PARIS, RHEA	Amics-M, BAMSE, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA, ROBBIC	Amics-M, BAMSE, BIB, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA	Amics-M, DARC, EDEN, GINI, MAS, PARIS, PIAMA, ROBBIC	Amics-M, BAMSE, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA	EDEN, MAS, PIAMA	Amics-M, DARC, GINI, LISA, PARIS, PIAMA	MAS, PIAMA	BAMSE, EDEN, PIAMA	Amics-M, GINI, LISA, MAS, PIAMA	MAS	PIAMA	BAMSE				✓
Smoking of adolescent																	
																	✓
Physical activity																	
																	✓

Table 4. (continued)

Variables	Follow-up	<1 year	1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years	11 years	12 years	13 years	14 years	15 years	MeDALL follow-up
Cooking with gas		Amics-M, BAMSE, DARC, EDEN, LISA, MAS, PARIS, PIAMA, ROBBIC	Amics-M, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, PIAMA	Amics-M, BIB, EDEN, GINI, INMA-S, INMA-V, LISA, PARIS, PIAMA	Amics-M, DARC, EDEN, PARIS, PIAMA, ROBBIC	Amics-M, INMA-S, INMA-V, LISA, PARIS, PIAMA	PARIS, PIAMA	Amics-M, DARC, GINI, LISA, PARIS	Amics-M, DARC, GINI, LISA, PARIS	BAMSE, EDEN		GINI, LISA	PIAMA					✓
		Amics-M, BAMSE, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA, ROBBIC	Amics-M, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, PIAMA	Amics-M, BIB, EDEN, GINI, INMA-S, INMA-V, LISA, PARIS, PIAMA	Amics-M, DARC, EDEN, PARIS, PIAMA, ROBBIC	Amics-M, INMA-S, INMA-V, LISA, PARIS, PIAMA	PARIS, PIAMA	Amics-M, DARC, GINI, LISA, PARIS	Amics-M, DARC, GINI, LISA, PARIS	BAMSE, EDEN		GINI, LISA	PIAMA					✓
		Amics-M, BAMSE, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA, ROBBIC	Amics-M, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, PIAMA	Amics-M, BIB, EDEN, GINI, INMA-S, INMA-V, LISA, PARIS, PIAMA	Amics-M, DARC, EDEN, PARIS, PIAMA, ROBBIC	Amics-M, INMA-S, INMA-V, LISA, PARIS, PIAMA	PARIS, PIAMA	Amics-M, DARC, GINI, LISA, PARIS	Amics-M, DARC, GINI, LISA, PARIS	BAMSE, EDEN		GINI, LISA	PIAMA					✓
		Amics-M, BAMSE, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA, ROBBIC	Amics-M, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, PIAMA	Amics-M, BIB, EDEN, GINI, INMA-S, INMA-V, LISA, PARIS, PIAMA	Amics-M, DARC, EDEN, PARIS, PIAMA, ROBBIC	Amics-M, INMA-S, INMA-V, LISA, PARIS, PIAMA	PARIS, PIAMA	Amics-M, DARC, GINI, LISA, PARIS	Amics-M, DARC, GINI, LISA, PARIS	BAMSE, EDEN		GINI, LISA	PIAMA					✓
		Amics-M, BAMSE, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, MAS, PARIS, PIAMA, ROBBIC	Amics-M, BIB, DARC, EDEN, GINI, INMA-S, INMA-V, LISA, PIAMA	Amics-M, BIB, EDEN, GINI, INMA-S, INMA-V, LISA, PARIS, PIAMA	Amics-M, DARC, EDEN, PARIS, PIAMA, ROBBIC	Amics-M, INMA-S, INMA-V, LISA, PARIS, PIAMA	PARIS, PIAMA	Amics-M, DARC, GINI, LISA, PARIS	Amics-M, DARC, GINI, LISA, PARIS	BAMSE, EDEN		GINI, LISA	PIAMA					✓
Variables were asked for the last 12 months.																		

the translations and back-translations of questionnaires were found to be correctly translated into the 8 other languages. However, it cannot be excluded that slightly different wording chosen in other languages has led to different interpretations. This might not be the case for questions about factual knowledge, such as ‘how many cigarettes do you smoke?’, but rather for questions on medical conditions such as ‘wheeze’, for which the general public understanding might be limited, and could lead to different answering behavior among participants. Also, asking for eczema – ‘have you (mother or father) ever had eczema?’ – highly depends on the patients’ understanding of the actual wording, which might also differ depending on the language used.

Moreover, the order of the harmonized questions within the questionnaire differs between the cohorts. As the cohorts should have the possibility to include their own questions, the harmonized questions are not asked in one exclusive part of the questionnaire, but are instead integrated in different sections of the cohorts’ own questionnaires. Not only the order, but also the way in which the questionnaires can be filled out varies in terms of using paper and pencil versus online completion. Furthermore, the age of the adolescents to which the questionnaire is given showed a discrepancy between the cohorts (14–18 years). No data will be retrieved for the age group 11–13 years within the MeDALL project. If the MeDALL-CQ is used in future studies, different ages of participants and the order of questions should be considered as one source of variability of the results.

The questionnaires were developed by the extraction of questions from former questionnaires, clinical experience, experience with specific questions in the cohort questionnaires and consensus in the research group, and, so far, a validation of the core questionnaires is missing. The MeDALL-CQ is an instrument under constant development and will be modified according to future experience and results.

Strengths and Generalizability

The harmonized MeDALL questionnaire, measuring a variety of health outcomes and possible determinants of allergies in childhood and adolescence, is publicly available in 9 different languages (Danish, Dutch, English, French, German, Greek, Italian, Spanish and Swedish) and has been used for the age groups 4–9 and 14–18 years.

For the 6 older birth cohorts, historical childhood data and the MeDALL-CQ will be harmonized to analyze longitudinal exposure-response relationships from childhood up to adolescence within the MeDALL project. The

separated parental and adolescent questionnaire versions allowed detailed use of the knowledge of each participant. While the parents were expected to give more reliable data on questions referring to conditions throughout the adolescent's life, housing situation and topics such as parental allergies, the adolescents were thought to be the more reliable source for information on current allergy symptoms, which can also occur without the knowledge of the parent, and on environmental exposures such as smoke exposure, which do not take place at home.

The 6 younger birth cohorts provided data up to 9 years of age in the current MeDALL follow-up. If the MeDALL-CQ is continuously used in the coming years, in the long-run these will be the cohorts with prospectively harmonized data, available from early childhood up to adolescence. Time-consuming data harmonization processes will be unnecessary in the future.

The construction of the ISAAC questionnaire was a major achievement in the field of asthma and allergy assessment, it encouraged networking between European cohorts, as in GA²LEN, and was the base on which many data harmonization projects such as ENRIECO have been built. MeDALL is taking this approach one step further by including a bigger pool of harmonized variables and using existing European birth cohorts as a data source with already existing historical data and further follow-ups planned for the coming years. MeDALL will offer a harmonized assessed multicountry sample of over 13,000 parent-child pairs.

Conclusion

The harmonized follow-up of 11 European birth cohorts in MeDALL will produce more comparable data across different cohorts and countries in Europe. In addition, all participating cohorts are allowed to include additional questions and instruments following their own special research interests, so that focused knowledge about specific local issues is obtained. The harmonized follow-up, however, does not reduce the need to harmonize historical data of the participating cohorts for combined longitudinal analyses.

Understanding geographical and time patterns of allergic diseases is a challenge. Results from the harmonized MeDALL follow-up will provide more insight into true differences or similarities between cohorts and/or countries in Europe. This new harmonized assessment will offer the possibility to verify results of former combined analyses for which otherwise extensive efforts of data harmonization are necessary. Thus, MeDALL can become the starting point to stringently plan, conduct and support future common asthma and allergy research initiatives in Europe.

Acknowledgments

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MeDALL

Mechanism of the Development of Allergy

Adolescent Questionnaire (age 14 - 18 years)

If parts or all of this questionnaire will be used, please refer to the origins of this questionnaire in all corresponding publications (see Supplement Fig. S4).



I) ASTHMA / WHEEZING

Core Questions

- 1 Have you had wheezing or whistling in the chest **in the past 12 months**?
☐ Yes ☐ No
- 2 How many attacks of wheezing have you had **in the past 12 months**?
☐ None
☐ 1 to 3
☐ 4 to 12
☐ More than 12
- 3 Have you had breathing difficulties (chest tightness, shortness of breath) **in the past 12 months**?
☐ Yes ☐ No
- 4 **In the past 12 months**, how often, on average, has your **sleep** been disturbed due to wheezing?
☐ Never woken with wheezing
☐ Less than one night per week
☐ One or more nights per week
- 5 **In the past 12 months**, has wheezing ever been severe enough to limit your **speech** to only one or two words at a time between breaths?
☐ Yes ☐ No
- 6 **In the past 12 months**, has your chest sounded wheezy during or after **exercise**?
☐ Yes ☐ No
- 7 **In the past 12 months**, have you had a **dry cough at night**, apart from a cough associated with a cold or chest infection?
☐ Yes ☐ No



- 8 Did you take any medicines for asthma or breathing difficulties (wheezing, chest tightness, shortness of breath) **during the last 12 months**?

(1) Prescription medication

☐ Yes ☐ No **If yes**, which? _____

- If you took oral cortical steroids, did you take them for **at least 3 days** in a row?

☐ Yes ☐ No

(2) Non-prescription medication

☐ Yes ☐ No **If yes**, which? _____

- 9 How would you estimate your complaints **in the past 12 months** due to wheezing/ breathing difficulties? (Place a vertical mark in the line below to indicate your complaints with wheezing.)

0 |-----| 10

(no complaints)

(the hardest complaints to imagine)

Supplemental Questions

- S1 1) In which **of the past 12 months** did the wheezing/breathing difficulties (chest tightness, shortness of breath) occur? (You may choose several answers) Please tick all months that apply:

☐ January	☐ April	☐ July	☐ October
☐ February	☐ May	☐ August	☐ November
☐ March	☐ June	☐ September	☐ December

- S2 How often did you suffer from breathing difficulties (chest tightness, shortness of breath) **in the past 12 months**?

☐ None
☐ 1 to 3
☐ 4 to 12
☐ More than 12

- S3 **In the past 12 months**, how often, on average, has your sleep been disturbed due to breathing difficulties (chest tightness, shortness of breath)?

☐ Never woken with breathing difficulties
☐ Less than one night per week
☐ One or more nights per week

- S4 **In the past 12 months**, have breathing difficulties (chest tightness, shortness of breath) ever been severe enough to limit your **speech** to only one or two words at a time between breaths?

☐ Yes ☐ No



S5 In the **past 12 months**, did you have breathing difficulties (chest tightness, shortness of breath) during or after **exercise**?

- ☐ Yes ☐ No
-

S6 If you have been taking asthma medication, how often do you take a relieving medication (e.g. ...) during a regular week?

- ☐ Less than 2 times a week
☐ 2 times or more a week
-

S7 How would you estimate your complaints **in the past month** due to wheezing/breathing difficulties? (Place a vertical mark in the line below to indicate your complaints with wheezing/breathing difficulties.)

0 |—————| 10
(no complaints) (the hardest complaints to imagine)

S8 In the **past 12 months**, which of these factors do you think triggered your wheezing or whistling in the chest? (You might choose several answers.)

- | | |
|--|---|
| ☐ Weather change (coldness, fog) | ☐ Tobacco smoke |
| ☐ Pollen | ☐ Emotion, stress |
| ☐ Gas exhaust, vapours, fumes | ☐ Tears, laughter, excitement |
| ☐ Dust | ☐ Wool clothes |
| ☐ Pets | ☐ Food or drink |
| ☐ Cold, flu or other respiratory infection | ☐ Soap, spray, cleaning product |
| ☐ Strong odours | ☐ Exercise (during or after) |

☐ Other (please specify): _____

S9 In the **last 12 months**, have you usually been congested in the chest or coughed up phlegm (mucus) when you **did not** have a cold?

- ☐ Yes ☐ No
-

S10 Are you congested in the chest or coughed up phlegm (mucus) on most days (4 or more days a week) for as much **as 3 months of the year**?

- ☐ Yes ☐ No



II) RHINITIS

Core Questions

- 10** In the **past 12 months**, have you had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu?

☐ Yes ☐ No

- 11** If yes, please specify which of the symptoms you had **in the past 12 months** when you DID NOT have a cold or the flu (You may choose several answers) Please tick all items that apply:

sneezing	☐ Yes	☐ No
runny nose	☐ Yes	☐ No
blocked nose	☐ Yes	☐ No

- 12** If yes, **in the past 12 months**, has this nose problem been accompanied by itchy-watery eyes?

☐ Yes ☐ No

- 13** In which of the **past 12 months** did this nose problem occur? (You may choose several answers) Please tick all months that apply:

☐ January	☐ April	☐ July	☐ October
☐ February	☐ May	☐ August	☐ November
☐ March	☐ June	☐ September	☐ December

- 14** In the **past 12 months**, did you have trouble with the nose or eyes (without having a cold) in association with one of the following? (You may choose several answers) Please tick all items that apply:

☐ animals
☐ grass, trees, flowers
☐ housedust, mite
☐ tobacco smoke or heavy scent
☐ air pollutants

☐ other, please specify _____

- 15** How would you estimate your complaints **in the past 12 months** due to nasal allergy/hay fever/allergic rhinitis? (Place a vertical mark in the line below to indicate your complaints with these problems.)

0 |—————| 10
(no complaints) (the hardest complaints to imagine)



16 Did you take any medications for nasal allergy/hay fever/allergic rhinitis **in the past 12 months?**

1) Prescription medication

☐ Yes ☐ No If yes, which? _____

2) Non-prescription medication

☐ Yes ☐ No If yes, which? _____

Chronic Rhino-Sinusitis (Fokkens et al. 2007 & 2012)

17 Has your nose been blocked during **the last 12 months?**

☐ Yes ☐ No

18 If yes, how long has your nose been blocked?

- ☐ Less than 10 days
☐ More than 10 days but less than 12 weeks
☐ 12 weeks or more
-

19 Have you had pain or pressure around the forehead, nose or eyes during **the last 12 months?**

☐ Yes ☐ No

20 If yes, how long have you had pain or pressure around the forehead, nose or eyes?

- ☐ Less than 10 days
☐ More than 10 days but less than 12 weeks
☐ 12 weeks or more
-

21 Have you had green or yellow nasal discharge (snot) or green or yellow mucus in the throat during **the last 12 months?**

☐ Yes ☐ No

22 If yes, how long have you had green or yellow nasal discharge (snot) or green or yellow mucus in the throat?

- ☐ Less than 10 days
☐ 10 days or more but less than 12 weeks
☐ 12 weeks or more
-

23 Have your sense of smell been reduced or absent during **the last 12 months?**

☐ Yes ☐ No



24 If yes, how long have your sense of smell been reduced or absent?

- ☐ Less than 10 days
☐ 10 days or more but less than 12 weeks
☐ 12 weeks or more

Supplemental Questions

ARIA-Criteria might be used for severity ratings but only apply to untreated patients:
(Bousquet et al., 2001)

S11 In the past 12 months, did you have trouble with your nose without having a cold for at least 4 days per week AND for at least 4 weeks?

- ☐ Yes ☐ No ("No" means less than 4 days per week OR less than 4 weeks)

S12 In the past 12 months, did this nose problem without having a cold interfere with your daily activities, sport or leisure time?

- ☐ Yes ☐ No

S13 Did you have abnormal sleep due to trouble with your nose without having a cold **during the last 12 months?**

- ☐ Yes ☐ No

S14 In the past 12 months, did this nose problem without having a cold interfere with your school or work?

- ☐ Yes ☐ No

III) ECZEMA

Core Questions

25 Have you had dry skin **in the past 12 months?**

- ☐ Yes ☐ No

26 Have you had an itchy rash at any time **in the past 12 months?**

- ☐ Yes ☐ No

27 Has this itchy rash at any time affected any of the following places
(You may choose several answers)? Please tick all that apply:

- | | |
|---|---|
| ☐ the folds of the elbows | ☐ under the buttocks |
| ☐ behind the knees | ☐ or around the neck, ears or face? |
| ☐ in front of the ankles | |

**Severity of Eczema**

28 Has this rash cleared completely at any time during **the past 12 months**?

- ☐ Yes ☐ No
-

29 In which **of the past 12 months** did this itchy rash/eczema occur?
(You may choose several answers.) Please tick all months that apply:

- | | | | |
|--------------------------------|-----------------------------|---------------------------------|--------------------------------|
| ☐ January | ☐ April | ☐ July | ☐ October |
| ☐ February | ☐ May | ☐ August | ☐ November |
| ☐ March | ☐ June | ☐ September | ☐ December |
-

30 In the **past 12 months**, how often, on average, have you been kept awake at night by this itchy rash?

- ☐ Never in the past 12 months
☐ Less than one night per week
☐ One or more nights per week
-

Contact Dermatitis

31 Have you ever had eczema on your hands (itchy lesions, blisters, rash)?

- ☐ Yes ☐ No

If yes, at which age was the onset? __ years

32 Have you ever had eczema after contact with:
(you may choose several answers, please tick all items that apply)

- ☐ items of metal (e.g. button, buckle, zipper, belt, watch or watchstrap, glasses or sun glasses, hair slide, cell phone, headset): please specify _____
- ☐ fashion jewellery
- ☐ hair dye
- ☐ other colourants
- ☐ tatoos
- ☐ cosmetics, perfume or fragrances
- ☐ deodorant
- ☐ shampoo or conditioner
- ☐ soap
- ☐ clothes
- ☐ latex, rubber (e.g. rubber gloves, balloons, preservatives)
- ☐ other materials, please specify: _____
- ☐ **no**, not with any material



Supplemental Questions

Please circle one response for each of the seven questions below. Children under 16 years should complete the questionnaire with the help of their parents. Please leave blank any questions you feel unable to answer.

(Charman et al., 2004)

-
- S15** **In the last 12 months,** on how many days in a typical week with eczema symptoms has your skin been itchy because of the eczema?
- ☐ No Days ☐ 1-2 Days ☐ 3-4 Days ☐ 5-6 Days ☐ Every Day
-
- S16** **In the last 12 months,** on how many nights in a typical week with eczema symptoms has your sleep been disturbed because of the eczema?
- ☐ No Days ☐ 1-2 Days ☐ 3-4 Days ☐ 5-6 Days ☐ Every Day
-
- S17** **In the last 12 months,** on how many days in a typical week with eczema symptoms has your skin been bleeding because of the eczema?
- ☐ No Days ☐ 1-2 Days ☐ 3-4 Days ☐ 5-6 Days ☐ Every Day
-
- S18** **In the last 12 months,** on how many days in a typical week with eczema symptoms has your skin been weeping or oozing clear fluid because of the eczema?
- ☐ No Days ☐ 1-2 Days ☐ 3-4 Days ☐ 5-6 Days ☐ Every Day
-
- S19** **In the last 12 months,** on how many days in a typical week with eczema symptoms has your skin been cracked because of the eczema?
- ☐ No Days ☐ 1-2 Days ☐ 3-4 Days ☐ 5-6 Days ☐ Every Day
-
- S20** **In the last 12 months,** on how many days in a typical week with eczema symptoms has your skin been flaking off because of the eczema?
- ☐ No Days ☐ 1-2 Days ☐ 3-4 Days ☐ 5-6 Days ☐ Every Day
-
- S21** **In the last 12 months,** on how many days in a typical week with eczema symptoms has your skin felt dry or rough because of the eczema?
- ☐ No Days ☐ 1-2 Days ☐ 3-4 Days ☐ 5-6 Days ☐ Every Day



IV) SOCIODEMOGRAPHIC CHARACTERISTICS

Core Questions

- 33** You are
☐ male ☐ female

- 34** What is your height? _____ cm
What is your weight? _____ kg

- 35** Which school degree did you achieve?
(define national levels / still in school/ left school without degree)

- 36** If you are still in school, which type of school are you in?
(define national types of school)

- 37** If you attend upper secondary school, which programme do you attend?
(ex. Science programme - Environment, Social studies - Economy,
Aesthetic programme - Dance, Handicraft programme - Hairdresser)
I attend: _____

- 38** Was your choice of school programme (upper secondary school or other school) affected by
asthma, allergic rhinitis, eczema or allergy?
☐ Yes ☐ No

- 39** How did your choice of programme get affected?



V) NUTRITION

Core Questions

Allergic Reactions to Food

40 Have you **ever** had an allergic reaction to food?

☐ Yes ☐ No

If yes, have you ever had an allergic reaction caused by... (You may choose several answers.)

41 **Cow's milk**

☐ Yes ☐ No Please describe the allergic reaction _____

How old were you when the allergic reaction to cow's milk first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

42 **Hen's egg**

☐ Yes ☐ No Please describe the allergic reaction _____

How old were you when the allergic reaction to hen's egg first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

43 **Wheat**

☐ Yes ☐ No Please describe the allergic reaction _____

How old were you when the allergic reaction to wheat first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

44 **Soy**

☐ Yes ☐ No Please describe the allergic reaction _____

How old were you when the allergic reaction to soy first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

**45 Codfish**

☐ Yes ☐ No Please describe the allergic reaction _____

How old were you when the allergic reaction to codfish first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

46 Peanut

☐ Yes ☐ No Please describe the allergic reaction _____

How old were you when the allergic reaction to peanut first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

47 Nuts other than peanut

☐ Yes ☐ No Please describe the allergic reaction _____

How old were you when the allergic reaction to peanut first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

48 If other food items have caused an allergic reaction, please specify food item:

Please describe the allergic reaction _____

How old were you when the allergic reaction to the food item first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

49 If other food items have caused an allergic reaction, please specify food item:

Please describe the allergic reaction _____

How old were you when the allergic reaction to the food item first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know



50 If other food items have caused an allergic reaction, please specify food item:

Please describe the allergic reaction _____

How old were you when the allergic reaction to the food item first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

VI) LIFESTYLE

Core Questions

The questions will ask you about the time you spent being physically active during a typical week in summer or winter. Please think about the activities you do at school or work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport. Please answer each question even if you do not consider yourself to be an active person.

Physical Activity (Craig et al., 2003)

51 During a typical week **in the last 12 months**, on how many hours did you do vigorous physical activities (lots of sweating, much harder breathing than normal, e.g. heavy lifting, digging, aerobics, or fast bicycling)?

summer _____ hours **per week**

winter _____ hours **per week**

52 During a typical week **in the last 12 months**, on how many hours did you do moderate physical activities (light sweating, slightly more breathing than normal, e.g. carrying light loads, bicycling at a regular pace, or swimming)?

summer _____ hours **per week**

winter _____ hours **per week**

53 During a typical week **in the last 12 months**, on how many hours did you do light physical activity (no sweating, normal breathing, e.g. walking)?

summer _____ hours **per week**

winter _____ hours **per week**

54 How many hours per day (**24 hours**) do you watch TV, read, use your computer or play computer- or TV-games?

summer _____ hours **per day**

winter _____ hours **per day**

Smoking

55 Do you smoke?

☐ Yes ☐ No



56 If yes, how many cigarettes are you smoking **per day**?

- ☐ ____ cigarettes per day ☐ not smoking on a daily basis
-

57 If you are not smoking on a daily basis, how many cigarettes are you smoking **per week**?

____ cigarettes per week

When did you start to smoke regularly (at least once a week)?

____ age in years

58 How often are you staying at indoor locations where someone smokes?

At home:

- ☐ Daily
☐ several days a week
☐ one day a week
☐ less than one day a week
☐ never

Not at home:

- ☐ Daily
☐ several days a week
☐ one day a week
☐ less than one day a week
☐ never
-

Alcohol and Drugs

59 Have you **ever** drunk alcohol?

- ☐ Yes ☐ no
-

60 If yes, how much alcohol did you drink on average **in the last 12 months**?

- ☐ beer
- ☐ 1 or more glasses per day
 - ☐ 5-6 glasses per week
 - ☐ 2-4 glasses per week
 - ☐ 1 glass per week
 - ☐ 1-3 glasses per months
 - ☐ <1 glass per month
 - ☐ never
- ☐ wine, sparkling wine
- ☐ 1 or more glasses per day
 - ☐ 5-6 glasses per week
 - ☐ 2-4 glasses per week
 - ☐ 1 glass per week
 - ☐ 1-3 glasses per months
 - ☐ <1 glass per month
 - ☐ never



- ☐ schnapps
- ☐ 1 or more glasses per day
 - ☐ 5-6 glasses per week
 - ☐ 2-4 glasses per week
 - ☐ 1 glass per week
 - ☐ 1-3 glasses per months
 - ☐ <1 glass per month
 - ☐ never

- ☐ alcopops, cocktails
- ☐ 1 or more glasses per day
 - ☐ 5-6 glasses per week
 - ☐ 2-4 glasses per week
 - ☐ 1 glass per week
 - ☐ 1-3 glasses per months
 - ☐ <1 glass per month
 - ☐ never

61 Have you **ever** taken drugs (e.g. marihuana, LSD, cocaine, ecstasy)?

- ☐ Yes ☐ No
-

62 If yes, how often did you take which drugs **in the last 12 months**?

- 1) _____ (name of drug), _____ (times of intake last 12 months)
- 2) _____ (name of drug), _____ (times of intake last 12 months)
- 3) _____ (name of drug), _____ (times of intake last 12 months)
-

VII) PUBERTY DEVELOPMENT (Carskadon et al., 1993)

Core Questions

The next questions are about changes that may be happening to your body. These changes normally happen to different young people at different ages. Since they may have something to do with your sleep patterns, do your best to answer carefully. If you do not understand a question or do not know the answer, just mark "I don't know."

63 Would you say that your growth in height:

- ☐ has not yet begun to spurt
- ☐ has barely started
- ☐ is definitely underway
- ☐ seems completed
- ☐ I don't know



64 And how about the growth of your body hair?
("Body hair" means hair any place other than your head, such as under your arms.)
Would you say that your body hair growth:

- ☐ has not yet begun to grow
 - ☐ has barely started to grow
 - ☐ is definitely underway
 - ☐ seems completed
 - ☐ I don't know
-

65 Have you noticed any skin changes, especially pimples?

- ☐ skin has not yet started changing
 - ☐ skin has barely started changing
 - ☐ skin changes are definitely underway
 - ☐ skin changes seem complete
 - ☐ I don't know
-

FORM FOR BOYS:

66 Have you noticed a deepening of your voice?

- ☐ voice has not yet started changing
 - ☐ voice has barely started changing
 - ☐ voice changes are definitely underway
 - ☐ voice changes seem complete
 - ☐ I don't know
-

67 Have you begun to grow hair on your face?

- ☐ facial hair has not yet started growing
 - ☐ facial hair has barely started growing
 - ☐ facial hair growth has definitely started
 - ☐ facial hair growth seems complete
 - ☐ I don't know
-

FORM FOR GIRLS:

68 Have you noticed that your breasts have begun to grow?

- ☐ have not yet started growing
 - ☐ have barely started growing
 - ☐ breast growth is definitely underway
 - ☐ breast growth seems complete
 - ☐ I don't know
-

69 Have you begun to menstruate (started to have your period)?

- ☐ Yes
- ☐ No

If yes, how old were you when you started to menstruate? ____ years and ____ months

Online suppl. FigS1. MeDALL Adolescent Core Questionnaire, 14-18 years.

Online suppl. FigS2. MeDALL Parental Core Questionnaire, 14-18 years.

Online suppl. FigS3. MeDALL Parental Core Questionnaire, 4-9 years.

Online suppl. FigS4. Detailed References for the Items of the MeDALL Core Questionnaires.

MeDALL

Mechanism of the Development of Allergy

Parental Questionnaire
(for parents of 14-18 year old children)

If parts or all of this questionnaire will be used, please refer to the origins of this questionnaire in all corresponding publications (see Supplement Fig. S4).



I) ASTHMA/WHEEZING

Core Questions

- 1 Has your child had wheezing or whistling in the chest **in the past 12 months**?
☐ Yes ☐ No
- 2 How many attacks of wheezing has your child had **in the past 12 months**?
☐ None ☐ 1 to 3 ☐ 4 to 12 ☐ More than 12
- 3 Has your child **ever** been diagnosed by a doctor as having asthma?
☐ Yes ☐ No
- 4 Has your child had a doctors diagnosis of asthma **in the past ____ years**
[each cohort should ask for time period not covered by this question since last follow-up]?
☐ Yes ☐ No
- 5 In the **past 12 months**, how often, on average, has your child's **sleep** been disturbed due to wheezing?
☐ Never woken with wheezing
☐ Less than one night per week
☐ One or more nights per week
- 6 In the **past 12 months**, has wheezing ever been severe enough to limit your child's **speech** to only one or two words at a time between breaths?
☐ Yes ☐ No
- 7 In the **past 12 months**, has your child's chest sounded wheezy during or after **exercise**?
☐ Yes ☐ No



- 8** In the **past 12 months**, has your child had a **dry cough at night**, apart from a cough associated with a cold or chest infection?

☐ Yes ☐ No

- 9** Did your child take any medicines for asthma or breathing difficulties (wheezing, chest tightness, shortness of breath) **in the last 12 months**?

(1) Prescription medication

☐ Yes ☐ No **If yes**, which? _____

- If your child took oral cortical steroids, did he/she take them for at least **3 days** in a row?

☐ Yes ☐ No

(2) Non-prescription medication

☐ Yes ☐ No **If yes**, which? _____

- 10** How often did you have to see a doctor or attend a hospital with your child **urgently** because of breathing difficulties (wheezing, chest tightness, shortness of breath) **in the last 12 months**?

Number: _____

Supplemental Questions

- S1** If your child received asthma medication, how often did he/she take a relieving medication (e.g. ...) during a **regular week**?

☐ Less than 2 times a week
☐ 2 times or more a week

- S2** Has your child **ever** been treated for **wheezing/breathing difficulties** (chest tightness, shortness of breath) with so called alternative methods (such as homoeopathy, acupuncture, others)?

☐ Yes ☐ No

- **If yes**, treatment with _____ started at age __ years and ended at __ years.
- Treatment with _____ started at age __ years and ended at __ years.
- Treatment with _____ started at age __ years and ended at __ years



S3 In the past 12 months, which of these factors do you think triggered your child's wheezing or whistling in the chest? (You might choose several answers.)

- | | |
|--|---|
| ☐ Weather change (coldness, fog) | ☐ Tobacco smoke |
| ☐ Pollen | ☐ Emotion, stress |
| ☐ Gas exhaust, vapours, fumes | ☐ Tears, laughter, excitement |
| ☐ Dust | ☐ Wool clothes |
| ☐ Pets | ☐ Food or drink |
| ☐ Cold, flu or other respiratory infection | ☐ Soap, spray, cleaning product |
| ☐ Strong odours | ☐ Exercise (during or after) |

☐ Other (please specify): _____

S4 In the last 12 months, has your child usually seemed congested in the chest or coughed up phlegm (mucus) when he/she did not have a cold?

- ☐ Yes ☐ No
-

S5 Does your child seem congested in the chest or cough up phlegm (mucus) on most days (4 or more days a week) for as much as 3 months of the year?

- ☐ Yes ☐ No



II) RHINITIS

Core Questions

- 11** In the **past 12 months**, has your child had problems with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu?
- ☐ Yes ☐ No
-
- 12** If yes, please specify which of the symptoms your child had **in the past 12 months** when he/she DID NOT have a cold or the flu (You may choose several answers) Please tick all items that apply:
- | | | |
|--------------|---------------------------|--------------------------|
| sneezing | ☐ Yes | ☐ No |
| runny nose | ☐ Yes | ☐ No |
| blocked nose | ☐ Yes | ☐ No |
-
- 13** If yes, **in the past 12 months**, has this nose problem been accompanied by itchy-watery eyes?
- ☐ Yes ☐ No
-
- 14** In which of the **past 12 months** did this nose problem occur? (You may choose several answers) Please tick all months that apply:
- | | | | |
|--------------------------------|-----------------------------|---------------------------------|--------------------------------|
| ☐ January | ☐ April | ☐ July | ☐ October |
| ☐ February | ☐ May | ☐ August | ☐ November |
| ☐ March | ☐ June | ☐ September | ☐ December |
-
- 15** In the **past 12 months**, did your child have trouble with the nose or eyes (without having a cold) in association with one of the following? (You may choose several answers) Please tick all items that apply:
- ☐ animals
 - ☐ grass, trees, flowers
 - ☐ housedust, mite
 - ☐ tobacco smoke or heavy scent
 - ☐ air pollutants
 - ☐ other, please specify _____
-
- 16** Did your child take any medications against nasal allergy/hay fever/allergic rhinitis **in the past 12 months**?
- 1) Prescription medication**
- ☐ Yes ☐ No If yes, which? _____
- 2) Non-prescription medication**
- ☐ Yes ☐ No If yes, which? _____



17 Did your child **ever** receive special injections against allergy ? ("allergy vaccine", immunotherapy, hyposensitization, desensitization, sublingual drops or tablets)

☐ Yes ☐ No

- If yes, first treatment started at age __ years and ended at __ years

☐ Against which allergen(s) _____ ☐ Not known

- Second treatment started at age __ years and ended at __ years

☐ Against which allergen(s) _____ ☐ Not known

- Third treatment started at age __ years and ended at __ years

☐ Against which allergen(s) _____ ☐ Not known

Supplemental Questions

S6 Was your child **ever** treated for nasal allergy/hay fever/allergic rhinitis with so called alternative methods (such as homoeopathy, acupuncture, others)?

☐ Yes ☐ No

- If yes, treatment with _____ started at age __ years and ended at __ years

- Treatment with _____ started at age __ years and ended at __ years

- Treatment with _____ started at age __ years and ended at __ years

III) ECZEMA

Core Questions

18 Has your child had dry skin **in the past 12 months**?

☐ Yes ☐ No

19 Has your child had an itchy rash at any time **in the past 12 months**?

☐ Yes ☐ No

20 Has this itchy rash at any time affected any of the following places (You may choose several answers)? Please tick all items that apply:

- ☐ the folds of the elbows
 - ☐ behind the knees
 - ☐ in front of the ankles
 - ☐ under the buttocks
 - ☐ or around the neck, ears or face?
-

21 Has this rash cleared completely at any time during **the past 12 months**?

☐ Yes ☐ No



- 22** Has your child ever been diagnosed by a doctor as having eczema/ atopic dermatitis/ neurodermatitis?
- ☐ Yes ☐ No
-
- 23** In which of **the past 12 months** did your child's eczema/itchy rash occur? (You may choose several answers) Please tick all months that apply:
- | | | | |
|--------------------------------|-----------------------------|---------------------------------|--------------------------------|
| ☐ January | ☐ April | ☐ July | ☐ October |
| ☐ February | ☐ May | ☐ August | ☐ November |
| ☐ March | ☐ June | ☐ September | ☐ December |
-
- 24** **In the past 12 months**, how often, on average, has your child been kept awake at night by this itchy rash?
- ☐ Never in the past 12 months
☐ Less than one night per week
☐ One or more nights per week
-
- 25** Has your child **ever** had eczema on her/his hands (itchy lesions, blisters, rash)?
- ☐ Yes ☐ No
- If yes, at which age was the onset? _ _ years (age in years)
-
- 26** Has your child **ever** had eczema after contact with (you may choose several answers, please tick all items that apply):
- ☐ items of metal (e.g. button, buckle, zipper, belt, watch or watchstrap, glasses or sun glasses, hair slide, cell phone, headset): please specify _____
 - ☐ fashion jewellery
 - ☐ hair dye
 - ☐ other colourants
 - ☐ tatoos
 - ☐ cosmetics, perfume or fragrances
 - ☐ deodorant
 - ☐ shampoo or conditioner
 - ☐ soap
 - ☐ clothes
 - ☐ latex, rubber (e.g. rubber gloves, balloons, preservatives)
 - ☐ other materials, please specify: _____
 - ☐ **no**, not with any material
-

Supplemental Questions

- S5** Was your child **ever** treated for nasal allergy/hay fever/allergic rhinitis with so called alternative methods (such as homoeopathy, acupuncture, others)?
- ☐ Yes ☐ No
- If yes, treatment with _____ started at age _ _ years and ended at _ _ years
- Treatment with _____ started at age _ _ years and ended at _ _ years
- Treatment with _____ started at age _ _ years and ended at _ _ years

IV) SOCIODEMOGRAPHIC CHARACTERISTICS

Core Questions

27 Your child is

☐ male ☐ female

28 Are you single parent?

☐ Yes ☐ No

29 Has the mother **ever** had **eczema** (excluding contact dermatitis and psoriasis)?

☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old were you at the onset of your eczema? _____ years

30 Has the mother **ever** had **asthma**?

☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old were you at the onset of your asthma? _____ years

31 Has the mother **ever** had hayfever or **allergic rhinitis**?

☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old were you at the onset of your allergic rhinitis/ hayfever? _____years

32 Has the father **ever** had **eczema** (excluding contact dermatitis and psoriasis)?

☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old was he at the onset of his eczema? _____ years

33 Has the father **ever** had **asthma**?

☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnose
☐ doctor- and self-diagnosed

If yes, how old was he at the onset of his asthma? _____ years

34 Has the father **ever** had hayfever or allergic rhinitis?

- ☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old were you at the onset of your allergic rhinitis/ hayfever? _____years

V) NUTRITION

Core Questions

35 Has your child ever had an allergic reaction to food?

- ☐ Yes ☐ No

If yes, has your child ever had an allergic reaction caused by...
(You may choose several answers.)

36 Cow's milk

- ☐ Yes ☐ No Please describe the allergic reaction _____

How old was your child when the allergic reaction to cow's milk first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

- ☐ Yes ☐ No ☐ I don't know

37 Hen's egg

- ☐ Yes ☐ No Please describe the allergic reaction _____

How old was your child when the allergic reaction to hen's egg first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

- ☐ Yes ☐ No ☐ I don't know

38 Wheat

- ☐ Yes ☐ No Please describe the allergic reaction _____

How old was your child when the allergic reaction to wheat first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

- ☐ Yes ☐ No ☐ I don't know

**39 Soy**

☐ Yes ☐ No Please describe the allergic reaction _____

How old was your child when the allergic reaction to soy first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

40 Codfish

☐ Yes ☐ No Please describe the allergic reaction _____

How old was your child when the allergic reaction to codfish first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

41 Peanut

☐ Yes ☐ No Please describe the allergic reaction _____

How old was your child when the allergic reaction to peanut first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

42 Tree nut

Yes No Please describe the allergic reaction _____

How old were you when the allergic reaction to peanut first occurred? _____ years

Do you still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

43 If other food items have caused reaction, please specify food item:

Please describe the allergic reaction _____

How old was your child when the allergic reaction to the food item first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know



44 If other food items have caused reaction, please specify food item:

Please describe the allergic reaction _____

How old was your child when the allergic reaction to the food item first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

If other food items have caused reaction, please specify food item:

45 Please describe the allergic reaction _____

How old was your child when the allergic reaction to the food item first occurred? _____ years

Does your child still have this allergic reaction when eating the food item?

☐ Yes ☐ No ☐ I don't know

VI) INDOOR ENVIRONMENT

Core Questions

46 Do you use gas for cooking?

☐ Yes ☐ No

47 Would you consider your house or flat as damp?

☐ Yes ☐ No

48 Is there mould or are there mould stains within your dwelling (except on food)?

☐ Yes ☐ No

If yes, in which rooms of your house or flat?

- ☐ Room or bedroom of the child
 - ☐ Rest of the flat
 - ☐ Basement
-

49 Does the child's mother smoke inside the home?

☐ Yes ☐ No If yes, number of cigarettes per day: _ _



50 Does the child's father smoke inside the home?

☐ Yes ☐ No If yes, number of cigarettes per day: _ _

51 Do others (except the child) smoke inside the home?

☐ Yes ☐ No If yes, number of cigarettes per day: _ _

52 Does the child smoke?

☐ Yes ☐ No If yes, number of cigarettes per day: _ _

MeDALL

Mechanism of the Development of Allergy

Parental Questionnaire
(for parents of 4-9 year old children)

If parts or all of this questionnaire will be used, please refer to the origins of this questionnaire in all corresponding publications (see Supplement Fig. S4).



I) Asthma/Wheezing

- 1 Has your child had wheezing or whistling in the chest **in the past 12 months**?
☐ Yes ☐ No
- 2 How many attacks of wheezing has your child had **in the past 12 months**?
☐ None
☐ 1 to 3
☐ 4 to 12
☐ More than 12
- 3 Has your child had breathing difficulties (chest tightness, shortness of breath) **in the past 12 months**?
☐ Yes ☐ No
- 4 **In the past 12 months**, has your child had a **dry cough at night**, apart from a cough associated with a cold or chest infection?
☐ Yes ☐ No
- 5 Has your child **ever** been diagnosed by a doctor as having asthma?
☐ Yes ☐ No
- 6 In the **past 12 months**, how often, on average, has your child's **sleep** been disturbed due to wheezing?
☐ Never woken with wheezing
☐ Less than one night per week
☐ One or more nights per week
- 7 **In the past 12 months**, has wheezing ever been severe enough to limit your child's **speech** to only one or two words at a time between breaths?
☐ Yes ☐ No
- 8 **In the past 12 months**, has your child's chest sounded wheezy during or after **exercise**?
☐ Yes ☐ No



- 9** In the past 12 months, how often has your child been disturbed by coughing/ wheezing/ whistling/ difficulty breathing when doing **exercise**?
- ☐ Never
 - ☐ Hardly ever
 - ☐ Less than half of the times
 - ☐ More than half of the times
 - ☐ Always or almost always (includes no exercising at all due to symptoms)
 - ☐ Does not make exercise due to other reasons
-
- 10** Has your child taken any medicines for asthma or breathing difficulties (chest tightness, shortness of breath) **in the last 12 months**? (include any inhalers, nebulisers, tablets or liquid medicines)
- ☐ Yes ☐ No
- ☐ If yes, which? _____
-
- 11** How often did you have to see a doctor or attend a hospital with your child **urgently** because of breathing difficulties (wheezing, chest tightness, shortness of breath) **in the last 12 months**?
- Number: _____
-

Supplemental Questions

- S1** Has your child ever had wheezing or whistling in the chest **at any time in the past**?
- ☐ Yes ☐ No
- ☐ If yes at what age did it occur? ____ months/years
-
- S2** In which month/s did this wheezing or whistling in the chest occur **in the past 12 months**? (You may choose several answers)
- | | | | |
|--------------------------------|-----------------------------|---------------------------------|--------------------------------|
| ☐ January | ☐ April | ☐ July | ☐ October |
| ☐ February | ☐ May | ☐ August | ☐ November |
| ☐ March | ☐ June | ☐ September | ☐ December |
-
- S3** In the past 12 months, which of these factors do you think triggered your child's wheezing or whistling in the chest? (You might choose several answers.)
- | | |
|--|---|
| ☐ Weather change (coldness, fog) | ☐ Tobacco smoke |
| ☐ Pollen | ☐ Emotion, stress |
| ☐ Gas exhaust, vapours, fumes | ☐ Tears, laughter, excitement |
| ☐ Dust | ☐ Wool clothes |
| ☐ Pets | ☐ Food or drink |
| ☐ Cold, flu or other respiratory infection | ☐ Soap, spray, cleaning product |
| ☐ Strong odours | ☐ Exercise (during or after) |
| ☐ Other (please specify): _____ | |



S4 In the past 12 months, how much did this wheezing interfere with your child's daily activities?

- ☐ Not at all
 - ☐ A moderate amount
 - ☐ A little
 - ☐ A lot
-

S5 Has your child had this wheezing or whistling in the chest been accompanied by an attack of breathlessness (dyspnoea) at least once in the past 12 months?

- ☐ Yes
 - ☐ No
-

S6 In the past 12 months, how many attacks of breathlessness has your child had?

- ☐ None
 - ☐ 1 to 3
 - ☐ 4 to 12
 - ☐ More than 12
-

S7 Has your child's sleep been disturbed due to an attack of breathlessness (dyspnoea) in the past 12 months?

- ☐ Yes
- ☐ No

If yes how often?

- ☐ Never woken with breathlessness
 - ☐ Less than one night per week
 - ☐ One or more nights per week
-

S8 If your child has had a dry cough at night and has been given bronchodilators (asthma relieving/ air passage widening medication) the effect of this medication on cough has been

- ☐ Rapid improvement (less than 30 minutes) although it could fade with time
 - ☐ Slow improvement (takes hours or days)
 - ☐ No improvement
 - ☐ Not used bronchodilators
-

S9 Have you ever given your child inhaled steroids?

- ☐ Yes
- ☐ No

If yes, how old was your child when s/he received inhaled steroids for the first time? ____

On average, how long did you give him (her) inhaled steroids since birth?

Specify the number of weeks: ____

S10 In the past 12 months, did you give your child oral steroids?

- ☐ Yes
- ☐ No



S11 Has your child **ever** been treated for **wheezing/breathing difficulties** with homoeopathy or acupuncture?

☐ Yes ☐ No

Cough and Phlegm

S12 **In the past 12 months**, has your child usually seemed congested in the chest or coughed up phlegm (mucus) with colds?

☐ Yes ☐ No

S13 **In the past 12 months**, has your child usually seemed congested in the chest or coughed up phlegm (mucus) when s/he did not have a cold?

☐ Yes ☐ No

S14 **In the past 12 months**, does your child seem congested in the chest or cough up phlegm (mucus) on most days (4 or more days a week) for as much as 3 months of the year?

☐ Yes ☐ No

S15 **In the past 12 months** has your child usually seemed congested in the chest or coughed up phlegm on most days (4 or more day a week) when s/he did not have a cold?

- ☐ No
☐ Yes, for less than 1 month a year
☐ Yes, for 1 or 2 months a year
☐ Yes, for 3 months a year or more
-

S16 **In the past 12 months** has a doctor said that your child has had a chest infection?

☐ Yes ☐ No



II) RHINITIS

- 12** In the **past 12 months**, has your child had problems with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu?
- ☐ Yes ☐ No
-
- 13** If yes, please specify which of the symptoms your child had **in the past 12 months** when he/she DID NOT have a cold or the flu. (You may choose several answers) Please tick all items that apply:
- | | | |
|--------------|---------------------------|--------------------------|
| sneezing | ☐ Yes | ☐ No |
| runny nose | ☐ Yes | ☐ No |
| blocked nose | ☐ Yes | ☐ No |
-
- 14** If yes, **in the past 12 months**, has this nose problem been accompanied by itchy-watery eyes?
- ☐ Yes ☐ No
-
- 15** In which of the **past 12 months** did this nose problem occur? (You may choose several answers) Please tick all months that apply:
- | | | | |
|--------------------------------|-----------------------------|---------------------------------|--------------------------------|
| ☐ January | ☐ April | ☐ July | ☐ October |
| ☐ February | ☐ May | ☐ August | ☐ November |
| ☐ March | ☐ June | ☐ September | ☐ December |
-
- 16** In the **past 12 months**, did your child have trouble with the nose or eyes (without having a cold) in association with one of the following? (You may choose several answers) Please tick all items that apply:
- | | | | |
|---|---------------------------|--------------------------|----------------------------------|
| ☐ animals, dust, mites | ☐ Yes | ☐ No | ☐ Don't know |
| ☐ grass, trees, flowers | ☐ Yes | ☐ No | ☐ Don't know |
| ☐ tobacco smoke | ☐ Yes | ☐ No | ☐ Don't know |
| ☐ housedust | ☐ Yes | ☐ No | ☐ Don't know |
| ☐ air pollutants | ☐ Yes | ☐ No | ☐ Don't know |
- (e.g. gas exhaust, vapours, fumes, spray, cleaning products, heavy scent)
- ☐ other, please specify _____
-
- 17** Did your child take any medications, tablets, nasal sprays or eye drops against nasal allergy/hay fever **in the past 12 months**?
- ☐ Yes ☐ No If yes, which? _____
-
- Has your child ever been diagnosed by a physician with having allergic rhinitis (rhinitis to cat, dust...) or hay fever (rhinitis to pollens)?
- ☐ Yes ☐ No



Supplemental Questions

S17 Has your child ever been treated for **nasal allergy/hay fever** with homoeopathy or acupuncture?

☐ Yes ☐ No

S18 **In the past 12 months**, how often has your child been disturbed by a runny/itchy/ blocked nose or itchy/watery/red eyes in the following activities?

☐ Sleep:	☐ Never	☐ very occasionally	☐ frequently	☐ most of the time
☐ School/homework:	☐ Never	☐ very occasionally	☐ frequently	☐ most of the time
☐ Outdoor activities:	☐ Never	☐ very occasionally	☐ frequently	☐ most of the time

III) ATOPIC DERMATITIS OR ECZEMA**Core Questions**

18 Has your child had dry skin **in the past 12 months**?

☐ Yes ☐ No

19 Has your child **ever** had an itchy rash which was coming and going for at least 6 months?

☐ Yes ☐ No

20 Has your child had an itchy rash which was intermittently coming and going at any time **in the past 12 months**?

☐ Yes ☐ No

21 Has this itchy rash at any time affected any of the following places (You may choose several answers)? Please tick all that apply:

- ☐ the folds of the elbows
 - ☐ behind the knees
 - ☐ in front of the ankles
 - ☐ under the buttocks
 - ☐ or around the neck, ears or face
-

22 Has this rash cleared completely at any time **during the past 12 months**?

☐ Yes ☐ No

23 Has your child **ever** been diagnosed by doctor with having eczema /atopic dermatitis?

☐ Yes ☐ No



24 In which of **the past 12 months** did your child's eczema/itchy rash occur? (You may choose several answers) Please tick all months that apply:

- | | | | |
|--------------------------------|-----------------------------|---------------------------------|--------------------------------|
| ☐ January | ☐ April | ☐ July | ☐ October |
| ☐ February | ☐ May | ☐ August | ☐ November |
| ☐ March | ☐ June | ☐ September | ☐ December |
-

25 In the past 12 months, how often, on average, has your child been kept awake at night by this itchy rash?

- ☐ Never in the past 12 months
☐ Less than one night per week
☐ One or more nights per week
-

Contact Dermatitis

26 Has your child **ever** had eczema on her/his hands (itchy lesions, blisters, rash)?

- ☐ Yes ☐ No

If yes, at which age was the onset? _ _ years

27 Has your child **ever** had eczema after contact with (You may choose several answers, please tick all items that apply):

- ☐ items of metal (e.g. button, buckle, zipper, belt, watch or watchstrap, glasses or sunglasses, hair slide, cell phone, headset): please specify _____
☐ fashion jewellery (earrings, rings...)
☐ colorants
☐ cosmetics, perfume or fragrances
☐ shampoo or conditioner
☐ soap
☐ clothes
☐ latex, rubber (e.g. rubber gloves, balloons)

☐ other materials, please specify: _____

☐ **no**, not with any material
-

Optional Supplemental Questions

Severity of Eczema

S19 Has your child **ever** been treated for eczema/atopic dermatitis with homoeopathy or acupuncture?

- ☐ Yes ☐ No



IV) FOOD ALLERGIC REACTIONS

Core Questions

- 28 Has your child ever had one or several abnormal reactions after eating a particular **food**?
☐ Yes ☐ No If yes, please tick any which apply. **See table on page 10!**
- 29 How old was your child when the allergic reaction first occurred? _____ years
- 30 Does your child still have this allergic reaction when eating the food item?
☐ Yes ☐ No ☐ I don't know
- 31 **In the last 12 months**, how often has your child been seen by a doctor for food reaction, **other than during or immediately after an actual episode**? (Please tick any which apply)
- | | Never | 1 to 3 | 4 to 12 | More than 12 |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| - Yes, by a general practitioner or a pediatrician | ☐ | ☐ | ☐ | ☐ |
| - Yes, by a pulmonologist or an allergist (hospital or office) | ☐ | ☐ | ☐ | ☐ |
| - Other (please specify): _____ | | | | |
- 32 **In the last 12 months**, how often has your child been hospitalized due to adverse food reactions?
_____ time(s) (If «no hospitalization», answer 0)
- 33 Did your child **ever** receive special injections or other treatments against allergy ("allergy vaccine"), immunotherapy, hyposensitisation or desensitisation?
☐ Yes ☐ No If yes, which allergen and when? _____

Supplemental Questions

- S20 If yes, first treatment started at age __ years and ended at __ years
Against which allergen(s) _____ ☐ Not known
Second treatment started at age __ years and ended at __ years
Against which allergen(s) _____ ☐ Not known
Third treatment started at age __ years and ended at __ years
Against which allergen(s) _____ ☐ Not known
(Cohorts that have asked this previously, should ask "since last follow-up" instead of "ever".)



Allergic reactions to medicine

34 Has your child ever had one or several abnormal reactions after taking a particular **medicine**?

☐ Yes ☐ No If yes, please tick all that apply. **See table on page 10!**

35 In the last 12 months, how often has your child been seen by a doctor for reactions to drugs, **other than during or immediately after an actual episode**? (Please tick any which apply)

	Never	1 to 3	4 to 12	More than 12
Yes, by a general practitioner or a pediatrician	☐	☐	☐	☐
Yes, by a pulmonologist or an allergist (hospital or office)	☐	☐	☐	☐
Other (please specify): _____				

36 In the last 12 months, how often has your child been hospitalized due to adverse food reactions?
_____ time(s) (If «no hospitalization», answer 0)

Allergic reactions to a vaccine

37 Has your child ever had one or several abnormal reactions after eating a particular **vaccination**?

☐ Yes ☐ No If yes, please tick any which apply. **See table on page 10!**

38 In the last 12 months, how often has your child been seen by a doctor for reactions to a vaccine, **other than during or immediately after an actual episode**? (Please tick any which apply)

	Never	1 to 3	4 to 12	More than 12
Yes, by a general practitioner or a pediatrician	☐	☐	☐	☐
Yes, by a pulmonologist or an allergist (hospital or office)	☐	☐	☐	☐
Other (please specify): _____				

39 In the last 12 months, how often has your child been hospitalized due to adverse vaccine reactions?

_____ time(s) (If «no hospitalization», answer 0)



Table to

IV) FOOD ALLERGIC REACTIONS

Nuts other than peanut

Questions:

Allergic reactions to food

No. 28

Allergic reactions to medicine

No. 34

Allergic reactions to vaccine

No. 37

FOOD												MEDICATION			
The child had the following reactions:	Fruit, vegetables	Milk	Egg white	Dried fruits	Peanut	Nuts other than peanut	Fish	Shellfish	Other food (please specify)	Drug (please specify)	Vaccine (please specify)	Insect stinging			
Face swelling	☐	☐	☐	☐	☐	☐	☐	☐				☐			
Lips swelling	☐	☐	☐	☐	☐	☐	☐	☐				☐			
Quincke's oedema	☐	☐	☐	☐	☐	☐	☐	☐				☐			
Generalized rash	☐	☐	☐	☐	☐	☐	☐	☐				☐			
Vomiting or diarrhea	☐	☐	☐	☐	☐	☐	☐	☐				☐			
Feeling of breathlessness	☐	☐	☐	☐	☐	☐	☐	☐				☐			
Faintness	☐	☐	☐	☐	☐	☐	☐	☐				☐			
Loss of consciousness	☐	☐	☐	☐	☐	☐	☐	☐				☐			
Excessive swelling around the bite site	☐	☐	☐	☐	☐	☐	☐	☐				☐			

**V) SOCIODEMOGRAPHIC CHARACTERISTICS**

40 Your child is

☐ male ☐ female

41 What is your child's height? ____ cm

What is your child's weight? ____ kg

42 Are you:

☐ Married (First marriage) ☐ Separated (but still legally married)
☐ Married (Second marriage) ☐ Divorced
☐ Single (never married) ☐ Widowed

43 Are you:

☐ Living with baby's other parent (father mother)
☐ Living with another partner
☐ Not living with a partner - but in a relationship
(eg partner living abroad or in another property)
☐ Not living with a partner and not in a relationship

44 Has the mother **ever** had **eczema** (excluding contact dermatitis and psoriasis)?

☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old were you at the onset of your **eczema**? ____ years

45 Has the mother **ever** had **asthma**?

☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old were you at the onset of your asthma? ____ years

46 Has the mother **ever** had hayfever or **allergic rhinitis**?

☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old were you at the onset of your allergic rhinitis/ hayfever? ____ years

47 Has the biological father **ever** had **eczema** (excluding contact dermatitis and psoriasis)?

- ☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old was he at the onset of his eczema? _____ years

48 Has the biological father **ever** had **asthma**?

- ☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnose
☐ doctor- and self-diagnosed

If yes, how old was he at the onset of his asthma? _____years

49 Has the biological father **ever had hayfever or allergic rhinitis?**

- ☐ Yes ☐ No If yes, ☐ doctor diagnosed
☐ self-diagnosed
☐ doctor- and self-diagnosed

If yes, how old were you at the onset of your allergic rhinitis/ hayfever? _____years

Supplemental Questions

S21 Since the last questionnaire, have you, or has a close relative been affected by:

- Serious health problems (e.g. chronic disease, depression, surgery, hospitalization)

Please specify the person(s) and the type of problem(s):

- Bereavement

S22 Since the last questionnaire, did you move?

- ☐ Yes ☐ No

S23 Since the last questionnaire, has there been a change in ...

- Your marital status?

- ☐ Yes, please specify: _____ ☐ No

- Your (or your partner's) occupational situation?

- ☐ Yes, please specify: _____ ☐ No



S24 Since the last questionnaire, has there been a new birth in your family?

☐ Yes, please specify when: _____ ☐ No

VI) NUTRITION

The cohort-specific Food Frequency Questionnaire for the measurement of nutrition will be used.

VII) AIR POLLUTION

The ESCAPE measurements will be used.

VIII) INDOOR ENVIRONMENT

Gas Stove

50 Do you use gas for cooking?

☐ Yes ☐ No

51 Do you have an extractor fan over the cooker?

☐ Yes ☐ No

If Yes, when cooking do you use the fan:

a) all of the time?	☐ Yes	☐ No
b) some o the time?	☐ Yes	☐ No
c) none of the time?	☐ Yes	☐ No

Dampness and Mould

52 Would you consider your house or flat as damp?

☐ Yes ☐ No

53 Is there mould or are there mould stains within your dwelling (except on food)?

☐ Yes ☐ No

54 If yes, in which rooms of the flat or house?

☐ Room or bedroom of the child
☐ Rest of the flat
☐ Basement

**Smoking**

55 Does the child's mother smoke inside the home?

☐ Yes ☐ No

If **occasionally**, number of cigarettes **per week** inside the home: __

If **regularly (every day)**, number of cigarettes **per day** inside the home: __

56 Does the child's father smoke inside the home?

☐ Yes ☐ No

If **occasionally**, number of cigarettes **per week** inside the home: __

If **regularly (every day)**, number of cigarettes **per day** inside the home: __

57 Do others (except the child) smoke inside the home?

☐ Yes ☐ No

If **occasionally**, number of cigarettes **per week** inside the home: __

If **regularly (every day)**, number of cigarettes **per day** inside the home: __

Supplemental Questions

S25 Is the child's mother currently smoking?

☐ Yes ☐ No ☐ Don't know ☐ Don't answer

If occasionally, number of cigarettes _____ **per week**.

S26 If yes, how many cigarettes does the child's mother smoke on average?

1. _____ cigarettes / **week**

2. _____ cigarettes / **day**

☐ Don't know ☐ Don't answer

S27 Is the child's father currently smoking?

☐ Yes ☐ No ☐ Don't know ☐ Don't answer

If occasionally, number of cigarettes _____ **per week**.

S28 If yes, How many cigarettes does the child's father smoke on average?

1. _____ cigarettes / **week**

2. _____ cigarettes / **day**

☐ Don't know ☐ Don't answer



S30 How often during a day is your child in a room or enclosed place (e.g. vehicle) where people are smoking:

Weekdays

- ☐ All the time
☐ More than 5 hours
☐ 3-5 hours
☐ 1-2 hours
☐ Less than 1 hour
☐ Not at all

Weekends

- ☐ All the time
☐ More than 5 hours
☐ 3-5 hours
☐ 1-2 hours
☐ Less than 1 hour
☐ Not at all

Physical Activity (Craig et al., 2003)

S31 How many hours on average **per day** does your child sleep INCLUDING naps?

_____ hours

S32 How much time on average per day does your child spend watching TV/DVDs or playing computer games? (for children aged older than 7 years)

Weekdays

Hours_____ Mins_____

Weekends

Hours_____ Mins_____

S33 During a typical week, what type of physical activities does your child do **outside the school**? Please specify the duration of each activity **per day**.

E.g. dancing, swimming lessons or running, bicycling, skating, going to a trip, etc.
(EXCLUDE Wii-sports and the journey to school).

*To go to a trip (information for nurses): please count the hours that the child walks during the trip. For example, if the child goes twice a month to a trip (with his/her parents, Scouts etc) please extrapolate the hours that the child spends doing physical exercise per week. E.g. If the child walks a total of 6h (3h per two Saturdays per month) it will be counted as 1h 30 min. per week.

Day	Activity(es)*	Hours	Minutes
E.g.:	Cycling 30m	0 1 2 3 4+	0 30
Monday	Swimming 30m	0 1 2 3 4+	0 30
Monday		0 1 2 3 4+	0 30
Tuesday		0 1 2 3 4+	0 30
Wednesday		0 1 2 3 4+	0 30
Thursday		0 1 2 3 4+	0 30
Friday		0 1 2 3 4+	0 30
Saturday		0 1 2 3 4+	0 30
Sunday		0 1 2 3 4+	0 30



- S34** During a typical week, what type of physical activities does your child do **during school time**, excluding activities during free time in the school yard? Please specify the duration of each activity per day.

Information for nurses: physical activity includes every programmed activity from physical education, swimming to dance lessons.

Day	Activity/es*	Hours	Mins
Monday		0 1 2 3 4+	0 30
Tuesday		0 1 2 3 4+	0 30
Wednesday		0 1 2 3 4+	0 30
Thursday		0 1 2 3 4+	0 30
Friday		0 1 2 3 4+	0 30
Saturday		0 1 2 3 4+	0 30
Sunday		0 1 2 3 4+	0 30

- S35** How much time during the day does your child spend on the schoolyard or playground?

_____ Hours

If your child has lunch at school, please include the time in hours spent on the playground or schoolyard after the meal.

_____ Hours

- S36** Do you know what kind of games does your child usually play on the playground/schoolyard?

☐ Yes ☐ No

If so, your child usually

- ☐ Sits down (taking, reading a book or playing sedentary games)
☐ Stands around or walk around
☐ Runs and plays a little bit
☐ Runs and plays quite a bit
☐ Runs and plays hard most of the time

Immunisations and Infections

- S37** Since the last questionnaire, has your child had one or several of the following infectious diseases:

- ☐ Chickenpox ☐ Scarlet fever ☐ Exanthematic disease
☐ Measles ☐ Mononucleosis
☐ Mumps ☐ Morbilliform
☐ Rubella pertussis ☐ Parotid disease

If yes, at what age? _____ years _____ months

Did this problem require, at least once, a consultation with a doctor?

☐ Yes ☐ No



S38 Which immunisations has your child received until now?
Add more rows as necessary

Vaccine	Date given (dd/mm/yy)

MeDALL

Mechanism of the Development of Allergy

Detailed References for the Items of the MeDALL Core Questionnaires



1

Parental Core Questionnaire, 4-9 year old children

ISAAC (The International Study of Asthma and Allergies in Childhood)

Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al.
International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods.
EUR RESPIR J 1995;8:483-491.

Questions 1-4, 6-8, 12, 13*, 14, 15, 19, 20 21*, 22, 24*, 25

IPAQ (International physical activity questionnaire)

Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE et al.
International physical activity questionnaire (IPAQ): 12-country reliability and validity.
MED SCI SPORTS EXERC. 2003;35(8):1381-95.

Questions S32-S34

Williams Working Criteria

Williams HC, Burney PG, Pembroke AC, Hay RJ.
The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent hospital validation.
BR J. DERMATOL 1994;131(3):406-16.

Question 18

ALSPAC (Avon Longitudinal Study of Parents and Children)

<http://www.bristol.ac.uk/alspac/researchers/resources-available/datadetails/questionnaires/documents/ques-cb07-my3-year-old-boy.pdf>

Question 30*

Questions stemming from former follow-ups of the MeDALL cohorts or were newly developed by a consensus of the MeDALL members

Questions 5, 9-11, 16, 17, 23, 26-56, 31 & S3, S4, S8-S11, S16-S29, S35-S38

Parental Core Questionnaire, about their 14-18 year old children

ISAAC (The International Study of Asthma and Allergies in Childhood)

Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al.
International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods.
EUR RESPIR J 1995;8:483-491.

Questions 1, 2, 5-8, 11, 12*, 13, 14, 19, 20*, 21, 23, 24 & S3-S5

Williams Working Criteria

Williams HC, Burney PG, Pembroke AC, Hay RJ. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent hospital validation.
BR J DERMATOL 1994;131(3):406-16.

Question 18

Questions stemming from former follow-ups of the MeDALL cohorts or were newly developed by a consensus of the MeDALL members

Questions 3, 4, 9, 10, 15-17, 22, 25-50 & S1, S2, S6, S7

**Adolescent Core Questionnaire, 14-18 years****ARIA (Allergic rhinitis and its impact on asthma)**

Bousquet J, van Cauwenberge P, Khaltaev N, in collaboration with the World Health Organization. Allergic Rhinitis and its Impact on Asthma.

J ALLERGY CLIN IMMUNOL 2001;108(5, SUPPL): 147-334.

Questions S11-S14

EPOS (European position paper on rhinosinusitis and nasal polyps)

Fokkens W, Lund V, Mullol J; European Position Paper on Rhinosinusitis and Nasal Polyps group. Chronic Rhinosinusitis with or without nasal polyps (CRSwNP or CRSsNP).

RHINOL SUPPL. 23; 2012; 50:1-298.

Fokkens W, Lund V, Mullol J, on behalf of the European Position Paper on Rhinosinusitis and Nasal Polyps group. EP3OS 2007: European position paper on rhinosinusitis and nasal polyps 2007. A summary for otorhinolaryngologists.

RHINOL 2007;45, 97-101

Retrieved via <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf> [accessed 20th Aug2012].

Questions 17-24

ISAAC (The International Study of Asthma and Allergies in Childhood)

Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al.

International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods.

EUR RESPIR J 1995;8:483-491.

Questions 1, 2, 4-7, 10, 11*, 12, 13, 26, 27*, 28-30 & S2*-S5*, S8-S10

IPAQ (International physical activity questionnaire)

Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE et al.

International physical activity questionnaire (IPAQ): 12-country reliability and validity.

MED SCI SPORTS EXERC. 2003;35(8):1381-95.

Questions 51-54

PDS (Pubertal Development Scale)

Carskadon MA, Acebo C. A self-administered rating scale for pubertal development.

JAH 1993;14:190-195.

Questions 63-69

POEM (Patient-Oriented Eczema Measure)

Charman CR, Venn AJ, Williams HC. The Patient-Oriented Eczema Measure development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective.

ARCH DERMATOL 2004;140(12):1513-1519.

Questions S15*-S21

VAS (Visual Analogue Scale)

Paul-Dauphin A, Guillemin F, Virion JM, Briançon S. Bias and precision in visual analogue scales: a randomized controlled trial.

AM J EPIDEMIOL 1999;150(10):1117-27.

Questions 9*, 15 & S7

Williams Working Criteria

Williams HC, Burney PG, Pembroke AC, Hay RJ. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent hospital validation.

BR J DERMATOL 1994;131(3):406-16.

Question 25

Questions stemming from former follow-ups of the MeDALL cohorts or were newly developed by a consensus of the MeDALL members

Questions 3, 8, 14, 16, 31-48, 53-61 & S1, S6